## REMARKS

The present application was filed on October 21, 2003, with 44 claims. In the Restriction Requirement of February 12, 2003, the Examiner requested election between composition claims 1-40 and method claims 41-45. On April 11, 2003, applicants elected composition claims 1-40; accordingly, claims 41-44 are restricted from the scope of this application.

In the Office Action under reply, pending claims 1-40 stand rejected as follows:

1. Claims 1-9, 12-16, 18-23, 26-32, 34, and 36-40 as anticipated under 35 U.S.C. § 102(b) by Shell et al. (U.S. Patent No. 5,972,389) ("the '389 Patent");
2. Claims 1-7, 10, 12, and 17-23 as anticipated under 35 U.S.C. § 102(b) by Shell (U.S. Patent No. 5,007,790) ("the '790 Patent");
3. Claims 1-7, 10, 17-22, and 39 as anticipated under 35 U.S.C. § 102(b) by Uemura et al. (U.S. Patent No. 4,695,467) ("Uemura et al.");
4. Claims 1-25, 39, and 40 as anticipated under 35 U.S.C. § 102(e) by Shell et al. (U.S. Patent No. 6,340,475) ("the '475 Patent"); and
5. Claims 33 and 35 as obvious under 35 U.S.C. § 103(a) over the '389 Patent in view of the '475 Patent.

Applicants acknowledge the Examiner's statement regarding the Information Disclosure Statement filed on April 7, 2003, and are submitting concurrently with this Amendment, a resubmission of the IDS complete with all non-patent literature cited therein.

Further, with respect to the Examiner's suggestion to change the term "cellulosic" in claims 6, 7, and 10 to "cellulose," on the grounds that the term "cellulosic" is not disclosed in the specification, applicants respectfully direct the Examiner's attention to page 20, line 15-16 and page 22, line 26 of the specification where the term "cellulosic" is used in the same context as it is used in claims 6, 7, and 10.

### THE CLAIM AMENDMENTS

With the present amendment, claim 1 has been amended and claims 45-54 are new. The amendment to claims 1 is made to further define the invention and does not include any previously unclaimed subject matter. Nevertheless, support for the recitation of claims 1 and 47 regarding the disintegration test and the use of USP disintegration equipment is found in the specification at *inter alia,* page 3, line 1 to page 5, line 8, and page 14, line 14 to page 16, line 27. Support for the recitation of claim 45 and 46 regarding the correlation of the active agent *in vivo* release profile to the active agent disintegration test *in vitro* release profile is found in the specification at page 3, lines 17-23. Support for the recitation of claims 48 and 49 regarding the ways to optimize the dosage form is found in the

specification at page 5, lines 28-29. Support for new claims 50-52 is found in the specification at Examples 1 and 2 and page 22, lines 11-21. Support for new claim 53 is found on the following pages of the specification: page 20, line 4; page 21, line 20 to page 22, line 3; and page 22, line 22. New independent claim 54 includes the subject matter of original claim 9, sans the word "optionally." In the Office Action under reply, the Examiner indicated that the subject matter of claim 9 would be allowable with the omission of the word "optionally" (*see*, Office Action, page 3, last para.). Upon entry of this Amendment, the following claims will be pending: claims 1-37, 39-40, and 45-54.

In addition to the foregoing, claims 41-44 have been canceled as drawn to a non-elected invention. This cancellation is made without prejudice and as such, applicants reserve the right to file one or more divisional applications on the canceled subject matter.

**THE '389 PATENT ANTICIPATION REJECTION**

Claims 1-9, 12-16, 18-23, 26-32, 34, and 36-40 stand rejected under 35 U.S.C. § 102(b) as anticipated by the '389 Patent. This rejection is moot for canceled claim 38 and is respectfully traversed for all applicable pending claims.

A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently, in a single prior art reference. *Minn. Mining & Mfg. Co. v. Johnson & Johnson Orthopaedics, Inc.*, 976 F.2d 1559, 1565, 24 USPQ2d 1321, 1326 (Fed. Cir. 1992). It is well-established that a product-by-process claim is a product claim that defines the claimed product in terms of the process by which it is made. *See, In re Luck*, 476 F.2d 650, 177 USPQ 523 (CCPA 1973); *In re Pilkington*, 411 F.2d 1345, 162 USPQ 145 (CCPA 1969); *In re Steppan*, 394 F.2d 1013, 156 USPQ 143 (CCPA 1967). The structure implied by the process steps should be considered when assessing the patentability of product-by-process claims over the prior art, especially where the product can only be defined by the process steps by which the product is made, or where the manufacturing process steps would be expected to impart distinctive structural characteristics to the final product. *See, e.g., In re Garnero*, 412 F.2d 276, 279, 162 USPQ 221, 223 (CCPA 1979).

As recited in claim 1, the present invention is directed to controlled release oral dosage form for administering a pharmacologically active agent to the stomach, duodenum, and upper small intestine of a patient, the dosage form comprising the pharmacologically active agent incorporated in a matrix of at leas0t one biocompatible, hydrophilic polymer that (a) swells in the presence of water in gastric fluid such that the size of the dosage form is sufficiently increased to provide gastric retention in the stomach of a patient in whom the fed mode has been induced, (b) gradually erode within the gastrointestinal tract over a determinable time period, and (c) release the active agent throughout the determinable time period,

wherein formulation of the dosage form includes subjecting the dosage form to a disintegration test for an extended period of time wherein the disintegration test is used to optimize the dosage form such that it has an *in vitro* active agent release profile that correlates to a desired *in vivo* active agent release profile for the dosage form. As explained on page 2-3 of the specification, the inventors of the present invention have found, surprisingly, that a disintegration test is a far more predictive test for drug release *in vivo* for controlled release dosage forms than are the dissolution tests generally used by those of ordinary skill in the art (page 2, lines 15-17; page 3, lines 1-4).

As explained on page 4 of the specification, drug release from the controlled release oral dosage form of the claimed invention is erosion controlled rather than swelling controlled. While the initial swelling rate of the dosage form may be initially greater than the erosion rate, during the course of administration of the oral dosage form, the erosion rate will generally surpass the swelling rate to deliver a full dose of the active agent. (Specification, page 4, line 26 to page 5, line 1.)

An advantage of the claimed controlled release oral dosage form is that it may be optimized to release the active agent from the swelled dosage form, via erosion, at a rate that is most beneficial to the patient. For example, as stated on page 5 of the specification, the dosage form may minimize or eliminate problems such as overgrowth of detrimental intestinal flora resulting from drugs that are toxic to normal intestinal flora, by delivering the bulk of the drug dose to the upper G.I. tract and allowing little or no drug to reach the lower G.I. tract or colon. The dosage form can also prevent chemical degradation of drugs by intestinal enzymes, loss of bioavailability of a drug due to its leaving the acidic environment of the stomach, and chemical degradation of a drug in the neutral to alkaline environment of the gastrointestinal tract. (Specification, page 5, lines 1-8.) As further explained on page 5 of the specification, the rate of diffusion of the active agent out of the matrix can be slowed relative to the rate at which the active agent is released via polymer erosion by increasing drug particle size and selecting a polymer that will erode faster than it will swell (lines 26-29). This disclosure is further elaborated at page 16, lines 19-20, where it is noted that the dosage form of the claimed invention may be optimized by different polymers, compositionally identical polymers having different molecular weights or different degrees of crosslinking (*see also*, page 14, lines 16-20).

The '389 Patent teaches a controlled-release or sustained-release gastric retentive oral dosage form wherein particles of a solid-state drug are dispersed in a swellable/erodible polymer, such as poly(ethylene oxide), and the drug is released into the stomach and duodenum at a rate dependent on the erosion rate of the polymer (col., 1, line 64, to col. 2, line 9). The molecular weight of the poly(ethylene oxide) is disclosed at ranging from about 900,000 to about 8,000,000, with a preferred molecular weight of 5,000,000. In Example 7, the molecular weight of the poly(ethylene oxide) is 2,000,000 in one tablet

and 5,000,000 in another tablet (col. 14, lines 13-17). While the disclosure of the '389 Patent teaches polymers that may be useful for the manufacture of the gastric retentive oral dosage form disclosed there, the '389 Patent does ***not*** teach or suggest the use of a test, such as a disintegration test, to optimize the disclosed oral dosage form for improved delivery of the drug to the stomach, duodenum, or the upper gastrointestinal tract.

As explained above and in the specification, through the use of the disintegration test, the inventors have found, surprisingly, that an improved controlled-release oral dosage form may be formulated. Because the disintegration test is use to improve the disintegration rate of the disclosed oral dosage form by altering the components of the dosage form, e.g., by changing the active agent particle size or by changing polymers, it follows that the use of the claimed disintegration test imparts *a structural advantage* to the claimed oral dosage form above and beyond those disclosed in the art at the time of the invention. *See, In re Garnero, supra.* Accordingly, because the '389 Patent does ***not*** teach or suggest the use of a disintegration test to optimize the disclosed oral dosage form, it follows that the '389 Patent does not anticipate or render obvious claims 1-9, 12-16, 18-23, 26-32, 34, 36, 37, 39, and 40, or new claims 45-54 of the present invention.

Turning to the additional features of new claims 50-54, the '389 Patent also does ***not*** teach or suggest: (i) combining two different molecular weight poly(ethylene oxide) polymers or copolymers as recited in claim 50; (ii) manufacturing the dosage form disclosed therein with a very low molecular weight poly(ethylene oxide) polymer, i.e., a poly(ethylene oxide) polymer with a molecular weight below 900,000, as recited in claim 53; or (iii) manufacturing the dosage form with a polymer matrix made of poly(ethylene oxide) admixed with poly(ethylene oxide-co-propylene oxide) as recited in claim 54.

Because the '389 Patent does not anticipate the claimed invention, applicants respectfully request reconsideration and withdrawal of this rejection.

**THE '790 PATENT ANTICIPATION REJECTION**

Claims 1-7, 10, 12, and 17-23 stand rejected under 35 U.S.C. § 102(b) as anticipated by the '790 Patent. This rejection is respectfully traversed for all applicable pending claims.

The '790 Patent is directed to a sustained-release oral drug-dosage form having a plurality of particles of a dispersion of a limited solubility drug in a hydrophilic, water-swellable, crosslinked polymer. Suitable crosslinked polymers for use in the '790 Patent are gelatin, albumin, sodium alginate, carboxymethyl cellulose, polyvinyl alcohol, and chitin (col. 3, ll. 13-14).

Similar to the '389 Patent discussed above, the '790 Patent does ***not*** teach or suggest that the dosage form disclosed therein may be optimized through the use of a disintegration test. Accordingly, it

follows that the '790 Patent does not anticipate or render obvious claims 1-7, 10, 12, and 17-23, or new claims 45-54 of the present invention.

Turning to the additional features of new independent claims 50-54, all of which disclose polyalkylene oxide matrices for the claimed oral dosage form, applicants note that the '790 Patent does ***not*** teach or suggest polyalkylene oxide polymers or copolymers as suitable polymers for crosslinking.

Because the '790 Patent does not anticipate the claimed invention, applicants respectfully request reconsideration and withdrawal of this rejection.

**THE UEMURA ET AL. ANTICIPATION REJECTION**

Claims 1-7, 10, 17-22, and 39 stand rejected under 35 U.S.C. § 102(b) as anticipated by Uemura et al. This rejection is respectfully traversed for all applicable pending claims.

Uemura et al. teaches a sustained-release tablet of wax-treated disintegrable granules containing: (a) a drug; (b) a disintegrating agent selected from the group consisting of starch derivatives, gums, cellulose derivatives, and ion-exchange resins; and (c) an excipient such as lactose, sucrose, and mannitol. To this combination, a water soluble polymer may be optionally added. Uemura et al. discloses the following as a list of optional water soluble polymers: (d) cellulose derivatives, synthetic water soluble polymers, and polysaccharides (col. 2, ll. 62-65; col. 3, ll. 10-18 and 38). Uemura et al. discloses polyethylene oxide as a synthetic water soluble polymer (col. 3, l. 37).

Like the '389 and the '790 Patent, Uemura et al. ***does*** not teach or suggest that the dosage form disclosed therein may be optimized through the use of a disintegration test. Accordingly, it follows that the '790 Patent does not anticipate or render obvious claims 1-7, 10, 17-22, and 39, or new claims 45-54 of the present invention.

Turning to the additional feature of new claims 50-52, Uemura et al. does ***not*** teach or suggest combining two or more poly(ethylene oxide) polymers or copolymers of different molecular weights, as recited in claim 50.

With respect to the additional feature of new independent claim 53, applicants note that Uemura et al. does ***not*** disclose a preferred molecular weight for the poly(ethylene oxide) disclosed at col. 3, line 37. Based upon established Federal Circuit precedent, applicants submit that the Uemura et al. Patent is ***not enabling*** for the disclosure of the poly(ethylene oxide) polymers.

On the issue of the enablement of references cited under 35 U.S.C. § 102, the Federal Circuit has held that in order to serve as a proper anticipatory reference, the reference must place the allegedly disclosed matter in the possession of the public. *Akzo N.V. et al. v. U.S. Int'l Trade Comm'n et al.*, 808 F.2d 1471, 1479 (Fed. Cir. 1986), *cert. denied*, 482 U.S. 909 (1987). Such possession is effected if one of

ordinary skill in the art can arrive at the claimed invention by combining the publication's description of the invention with the ordinary artisan's knowledge. *In re Donohue,* 766 F.2d 531, 533 (Fed. Cir. 1985). Under this rubric, even if the claimed invention is disclosed in a printed publication, the disclosure will not be proper prior art under 35 U.S.C. § 102 if it is not enabling. *Id.* The Federal Circuit has explained that in order for a disclosure to be enabling, "the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without 'undue experimentation.'" *Enzo Biochem, Inc. v. Calgene, Inc.,* 188 F.3d 1362, 1371 (Fed. Cir. 1999). To constitute adequate enablement, the specification, *not* the knowledge of one skilled in the art, must supply the novel aspects of the invention. *Genentech, Inc. v. Novo Nordisk et al.,* 108 F.3d 1361 (Fed. Cir. 1997) (emphasis added here). The Federal Circuit emphasized this important point when it stated:

> Tossing out the mere germ of an idea does not constitute enabling disclosure...reasonable detail must be provided in order to enable members of the public to understand and carry out the invention. *Id.*

Within the description and examples of Uemura et al., no guidance is provided for preparing the disintegrable granules disclosed therein with poly(ethylene oxide). On this matter, it is important to note that all of the Examples of Uemura et al. use hydroxypropylmethylcellose as the polymer for the preparation of the disintegrable granules (*see*, Examples 1-11). Thus, it follows that the Uemura et al. is ***not*** enabling for the preparation of the disintegrable granules disclosed therein with a poly(ethylene oxide) polymer of any particular weight.

Even assuming *arguendo* that the ordinary artisan would be able to fashion the disintegrable granules of Uemura et al. using what was known in the art at the time of that the subject matter of the Uemura et al. patent was invented, applicants submit that the ordinary artisan would not be led to produce the disintegrable granules with a low molecular weight poly(ethylene oxide) polymer. In support of this contention, the Examiner need only turn to the disclosure of the'790 Patent, which demonstrates that as late as 1999, it was the state of the art to use poly(ethylene oxide) polymers having a molecular weight of at least 900,000, with molecular weights in excess of 900,000 preferred for the production of pharmacological matrices. Based upon the foregoing analysis, it follows that Uemura et al. is ***not*** enabling for a polymer matrix comprised of a poly(ethylene oxide) having a molecular weight below 900,000, as recited in claim 53.

With respect to the additional feature of new independent claim 54, Uemura et al. does ***not*** teach or suggest a dosage form that includes a polymer matrix made of poly(ethylene oxide) admixed with poly(ethylene oxide-co-propylene oxide), as recited in claim 54.

Because Uemura et al. does not anticipate any of the claims of the instant application, applicants respectfully request reconsideration and withdrawal of this rejection.

**THE '475 PATENT ANTICIPATION REJECTION**

Claims 1-25, 39, and 40 stand rejected under 35 U.S.C. § 102(e) as anticipated by the '475 Patent. This rejection is respectfully traversed for all applicable pending claims.

The '475 Patent is directed to a unit oral dosage form comprising a highly soluble drug in a hydrophilic polymer that swells upon imbibation of water to a size that is large enough to promote retention of the dosage form in the stomach during the fed mode. Poly(ethylene oxide) is disclosed as a suitable polymer for use in the '475 Patent. The molecular weight of the poly(ethylene oxide) is disclosed as ranging from 10,000 to about 10,000,000 (col. 8, ll. 40-42).

Like the '389, the '790 Patent, and Uemura et al., the '475 Patent ***does*** not teach or suggest that the dosage form disclosed therein may be optimized through the use of a disintegration test. Accordingly, it follows that the '475 Patent does not anticipate or render obvious claims 1-7, 10, 17-22, and 39, or new claims 45-54 of the present invention.

Turning to the additional feature of new claims 50-52, the '475 Patent does ***not*** teach or suggest combining two different molecular weight poly(ethylene oxide) polymers or copolymers, as recited in claim 50.

With respect to the additional feature of new claim 53, applicants direct the Examiner's attention to MPEP § 716.10 (titled "Attribution"), which provides the following guidance on anticipation rejections under 35 U.S.C. § 102(e):

> Under certain circumstances an affidavit or declaration may be submitted which attempts to attribute an activity, a reference or part of a reference to the applicant. If successful, the activity or the reference is no longer applicable. MPEP § 716.10 (8th Ed. Rev. 1, pp. 700-249 to 700-250 (Feb. 2003)).

The MPEP explains in the same section that an affidavit or declaration by one inventor of the prior reference and the subject application may be sufficient to eliminate the prior reference or subject matter from the prior reference as prior art.

In the instant case, the attached Declaration of inventor Jenny Louie-Helm presents evidence that Dr. Louie-Helm is the inventor of the low molecular weight polymers that are claimed in both the '475 Patent and the instant application. In this Declaration, Dr. Louie-Helm explains that those polymers having molecular weights below 900,000 are considered to be very low molecular weight polymers.

Accordingly, with this Declaration, the low molecular weight polymers of the '475 Patent are removed as prior art for the claimed invention.

With respect to the additional feature of new claim 54, the '475 Patent does ***not*** teach or suggest a dosage form that includes a polymer matrix comprised of poly(ethylene oxide) admixed with poly(ethylene oxide-co-propylene oxide).

Because the '475 Patent does not anticipate any of the claims of the instant application, applicants respectfully request reconsideration and withdrawal of this rejection.

**THE '389 PATENT OBVIOUSNESS REJECTION**

Claims 33 and 35 stand rejected under 35 U.S.C. § 103(a) as obvious over the '389 Patent in view of the '475 Patent. This rejection is rendered moot for the reason that follows.

As noted above in the anticipation discussion of the '389 Patent, the '389 Patent does ***not*** teach or suggest using a disintegration test to optimize the dosage form disclosed therein. Claims 33 and 35 ultimately depend from independent claim 1. Because the '389 Patent alone does not render obvious independent claim 1, it follows that dependent claims 33 and 35 are also not rendered obvious by the '389 Patent alone.

The Examiner cites the '475 Patent for the disclosure of metformin in combination with a hydrophilic swellable polymer. The '475 Patent is owned by DepoMed, Inc., which is also the owner of the instant application. Because the '475 Patent and the instant application are both co-owned by DepoMed, the '475 Patent may not be cited as prior art against the instant application in an obvious rejection pursuant to 35 U.S.C. § 103(c), which reads as follows:

> Subject matter developed by another person, which qualifies as prior art only under one or more of subsections (e), (f), and (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

Pursuant to MPEP § 706.02(l)(3), applicants submit the following Statement of Common Ownership between the instant application and the '475 Patent.

**STATEMENT OF COMMON OWNERSHIP**

The instant Application, U.S. Patent Application No. 10/014,750, filed on October 25, 2001, and U.S. Patent No. 6,340,475, filed on March 29, 1999, and issued on January 22, 2002, were both owned by DepoMed, Inc. at the time of the invention of the instant application, U.S. Patent Application No. 10/014,750.

With this Statement of Common Ownership, the '475 Patent is excluded as prior art under 35 U.S.C. § 103(a) against the instant application.

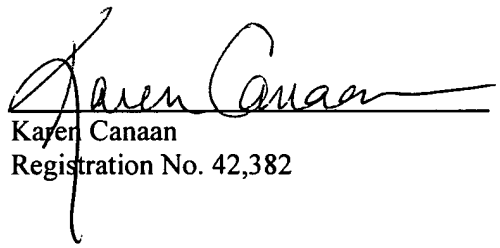
Accordingly, because claims 33 and 35 are not rendered obvious by the '389 Patent alone, applicants respectfully request reconsideration and withdrawal of this rejection.

## CONCLUSION

The foregoing discussion distinguishes the claimed invention over each of the cited references and addresses all of the Examiner's objections to the application. As all of the outstanding rejections and objections for this application have been overcome and addressed, applicants respectfully request withdrawal of all claim rejections and objections and passage of this application to issue.

Should the Examiner wish to contact the undersigned to discuss this response or the application in general, she is welcome to do so at 650-330-4913 or at canaan@reedpatent.com.

Respectfully submitted,

By: 
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